Remarks

Claims 1 to 3 and 6 to 15 were pending. By this Amendment, claims 6 and 8 were amended. No new matter has been added thereby and accordingly entry of the amendments is respectfully requested. Claims 1 to 3 and 6 to 15, as amended, are now pending and before the Examiner.

The Examiner rejected claim 6 as allegedly indefinite under 35 U.S.C. § 112, second paragraph.

In response, applicants have amended claim 6 and maintain that such amendment renders the Examiner's rejection moot. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner rejected claims 1 to 3 and 6 to 14 as allegedly obvious under 35 U.S.C. § 103(a) over Friedl *et al.* (U.S. Patent Publication No. 2005/0089575) in view of Frisbee *et al.* (WO 99/17744). The Examiner also rejected claims 1, 14, and 15 as allegedly obvious under 35 U.S.C. § 103(a) over Friedl *et al.* in view of Frisbee *et al.*, and further in view of Gendron *et al.* (U.S. Patent Publication No. 2002/0137678), Parikh (Handbook of Pharmaceutical Granulation Technology), and the EPA Profile of the Pharmaceutical Manufacturing Industry ("EPA Profile").

Applicants respectfully traverse the rejections. Since Friedl *et al.* forms the basis for both obviousness rejections, applicants will discuss the content of Friedl *et al.* first and then explain why the secondary references do not provide the necessary teachings for what Friedl *et al.* lacks to make a proper obviousness rejection. This is not attacking the references individually, as the Examiner alleges, but the clearest way of explaining why the cited references <u>when combined</u> do not render the instant invention obvious.

Thus, Friedl *et al.* does not teach or suggest the use of "poloxamers having an average molecular weight of about 2000 to 12000", as the pending claims require. The claimed invention is based on the finding that the speed and extend of dissolution of the active agent telmisartan is unexpectedly improved by combining a basic agent and a poloxamer. Thus, in a test dissolution assay (pH 4.0) more than 75% of 40 mg telmisartan was dissolved after 30

minutes if in the presence of 40 mg meglumine and 4% poloxamer Pluronic 68, while less than 50% was dissolved in the same time period in the same formulation lacking the poloxamer. After 60 minutes, in the presence of poloxamer about 80% of telmisartan had been dissolved, whereas in the same time period, in the absence of poloxamer, only 55% had dissolved. Friedl *et al.* does not teach, suggest, or hint at such an unexpected and valuable advantage of the claimed invention.

It should also be noted that Friedl *et al.* considered surfactants and emulsifiers as optional and not essential excipients, because the manufacturing process of Friedl *et al.* relies on spray-drying. The compositions described in Friedl *et al.* are unsuitable for the simpler fluid bed granulation process. Thus, the preferred amount of surfactant (0.05-1%) mentioned in Friedl *et al.* at paragraph [0058] is quite different from the preferred amount according to the present invention. Since these are the preferred amounts, Friedl *et al.* accordingly provides no motivation for one of skill in the art to use the amount of surfactants and emulsifiers similar to those of the claimed invention and the Examiner has set forth no such motivation to use these optional emulsifiers or more of them than is considered preferred. Furthermore, the hygroscopicity of the tablets made according to the instant claims are very low up to 80% RH. In contrast, the hygroscopicity of the tablets made according to Friedl *et al.*, even in low RH conditions, is higher, which means that the instant claimed invention has an advantage for handling the tablets and provides a significant product and marketing advantage. Furthermore, the coating of carrier particles in a fluidized bed as mentioned in Friedl *et al.* is not the same as fluid-bed granulation referred to as the preferred formulation technique in the claimed invention as this technique does not involve the coating of particles with telmisartan.

Nor does Frisbee *et al.* provide what Friedl *et al.* lacks. Frisbee *et al.* does not disclose the use of telmisartan or sartans at all. It is unclear why one would consider the formulations of Frisbee *et al.* even useful for telmisartan or sartans generally, much less than its teachings could modify that of Friedl *et al.*, much less with a reasonable expectation of success. Accordingly, since both obviousness rejections require such missing teaching from Frisbee *et al.*, both rejections should be reconsidered and withdrawn on this basis alone.

Furthermore, Gendron *et al.*, Parikh, or the EPA Profile art do not provide what Friedl *et al.* or Frisbee *et al.* lacks. For example, it is improbable that Gendron *et al.* would be consulted

by a person skilled in the art at all, because Gendron *et al.* specifically relates to proteinaceous substances as active agents, which would not include telmisartan. Therefore, like Frisbee *et al.*, Gendron *et al.* itself provides no basis for concluding that it teachings would be suitable for telmisartan or sartans at all and could properly and reasonably modify the teachings of Friedl *et al.* or Frisbee *et al.*, much less with a reasonable expectation of success. Moreover, paragraph [0072] does not teach that Pluronics or other specified compounds have been known to improve the solubility of poorly water-soluble compounds in general but just that these Pluronics or other specified compounds can be used as co-solvents for tbdn-1 agents of limited solubility and are commercially available. There is no indication or hint that this teaching concerning tbdn-1 agents of limited solubility is somehow applicable to compounds such as telmisartan. Furthermore, there is no teaching or hint of the specific poloxamers of claim 6. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejection.

The Examiner also provisionally rejected claims 1 to 3 and 6 to 13 for nonstatutory obviousness-type double patenting over claims 1 to 13 of U.S.S.N. 11/560,059, in view of Frisbee *et al.*

In response, applicants undertake to file a terminal disclaimer with respect to U.S.S.N. 11/560,059, if (1) the instant claims be found otherwise allowable, and (2) applicants determine that such application poses a double patenting issue at that time. Since the scope of the claims may change and moot the provisional rejection, there is not need to address this issue at this time. Accordingly, applicants respectfully request that the Examiner withdraw the provisional rejection for consideration later.

Applicants submit that all the pending claims are allowable and respectfully solicit a Notice of Allowance for all of the pending claims. If the Examiner feels that a telephone interview would be helpful in advancing prosecution of this application, the Examiner is invited to contact the attorney below.

Respectfully submitted,

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